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(51) International Patent Classification⁵ : A61K 31/47, 31/535, 31/495 C07D 491/056, 215/233, 215/26 // C07D 491/056, 317/00, 221/00	A3	(11) International Publication Number: WO 94/02145 (43) International Publication Date: 3 February 1994 (03.02.94)
(21) International Application Number: PCT/US93/06893 (22) International Filing Date: 22 July 1993 (22.07.93) (30) Priority data: 918,824 22 July 1992 (22.07.92) US (60) Parent Application or Grant (63) Related by Continuation US 918,824 (CIP) Filed on 22 July 1992 (22.07.92) (71) Applicants (for all designated States except US): GENEL-ABS TECHNOLOGIES, INC. [US/US]; 505 Penobscot Drive, Redwood City, CA 94063 (US). THE UNIVERSITY OF NORTH CAROLINA [US/US]; CB #4100, 300 Bynum Hall, Chapel Hill, NC 27599-4100 (US). (72) Inventors; and (75) Inventors/Applicants (for US only) : LEE, Kuo-Hsiung [US/US]; 1426 Gray Bluff Trail, Chapel Hill, NC 27514 (US). KUO, Sheng-Chu [-/-]; 5th Floor, 19 Lane 238, Szu-Ping Ro, Tai-Chung (TW). WU, Tian-Shung [-/-]; 257 Hsi-Men Road, Section 2, Taiwan City, 70107 (TW). LIU, Su-Ying [-/US]; 1004 Misty Lane, Belmont, CA 94002 (US). HWANG, Kou, M. [US/US]; 220 Stanbridge Court, Danville, CA 94526 (US). WENG, Hui, Kang [CN/US]; 105 Fidelity Street, Apt. B35, Carrboro, NC 27510 (US). LI, Le, Peng [CN/US]; 302 Mason Farm Road, Apt. A, Chapel Hill, NC 27514 (US).		(74) Agent: POWERS, Vincent, M.; Law Offices of Peter J. Dehlinger, P.O. Box 60850, Palo Alto, CA 94306-0850 (US). (81) Designated States: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 28 April 1994 (28.04.94)
(54) Title: 2-ARYL-4-QUINOLONES AS ANTITUMOR COMPOUNDS <div style="text-align: center;"> <p>(Ia)</p> </div> (57) Abstract A method of inhibiting tumor-cell growth, by administering a pharmaceutically effective amount of a 2-aryl-4-quinolone compound, is disclosed. The 2-aryl-4-quinolone compound is effective to inhibit tumor cell growth in tumors in which multiple drug resistance is encountered. Also disclosed are novel 2-aryl-4-quinolone anti-tumor compounds.		

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INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER IPC 5 A61K31/47 A61K31/535 A61K31/495 C07D491/056 C07D215/233 C07D215/26 //C07D491/056,317/00,221/00		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 5 A61K C07D		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP-A-0 341 104 (LIPHA) 8 November 1989	1-7, 11, 12, 15, 16
Y	see the whole document ---	1-18
P, X	J. MED. CHEM., vol. 36, no. 9, 30 April 1993 pages 1146 - 1156 K. SHENG-CHU 'Synthesis and cytotoxicity of 1,6,7,8-substituted 2-(4'-substituted phenyl)-4-quinolones and related compounds: Identification as antimitotic agents interacting with tubulin'	1-7, 11, 12, 15, 16
Y	see the whole document --- -/--	1-18
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents : 'A' document defining the general state of the art which is not considered to be of particular relevance 'E' earlier document but published on or after the international filing date 'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) 'O' document referring to an oral disclosure, use, exhibition or other means 'P' document published prior to the international filing date but later than the priority date claimed 'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention 'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone 'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. '&' document member of the same patent family		
Date of the actual completion of the international search		Date of mailing of the international search report
6 December 1993		29. 03. 94
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016		Authorized officer KRAUTBAUER, B

INTERNATIONAL SEARCH REPORT

Int. l. Application No

PCT/US 93/06893

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Y	see the whole document ---	1-18
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X	TETRAHEDRON LETTERS, vol.33, no.3, 14 January 1992 pages 373 - 376 V.N. KALININ ET AL. 'A new route to 2-aryl-4-quinolones via palladium-catalyzed carbonylative coupling of o-iodoanilines with terminal arylacetylenes'	11,12, 15,16
Y	see the whole document ---	1-18
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D,X	CHEM. IND., no.4, 1981 page 121 A. KASAHARA ET AL. 'A new synthesis of 2-aryl-4-quinolones'	11,12
Y	see the whole document ---	1-18
Y	J. MED. CHEM., vol.33, 1990 pages 1721 - 1728 J.B. JIANG ET AL. 'Synthesis and biological evaluation of 2-styrylquinazolin-4(3h)-ones, a new class of antimitotic anticancer agents which inhibit tubulin polymerization'	1-10
2 X	EP-A-0 343 574 (KIRIN BEER KABUSHIKI KAISHA) 29 November 1989	11,12, 15,16
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INTERNATIONAL SEARCH REPORT

Int. l. Application No.

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C.(Continuation) D. CUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US-A-5 126 351 (M.J. LUZZIO ET AL.) 30 June 1992 see the whole document ---	1-10
Y	US-A-3 725 413 (J. GENZER ET AL.) 3 April 1973 see the whole document ---	8-10, 13, 14, 17, 18
Y	FR-A-2 276 049 (CHINOIN GYOGYSZER ES VEGYESZETI TERMEKEK GYARA RT.) 23 January 1976 see the whole document ---	8-10, 13, 14, 17, 18
Y	DATABASE WPI Week 8112, Derwent Publications Ltd., London, GB; AN 81-20215D & JP-A-56 007 784 (YOSHITOMI PHARM IND KK) 27 January 1981 see abstract -----	1-10

INTERNATIONAL SEARCH REPORT

International application No.

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.: **X**
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Please see explanations mentioned in form PCT/ISA/206 dated 12.01.94.
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

For further information please see form PCT/ISA/206 dated 12.01.1994.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-18

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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		CA-A- 1325205	14-12-93
		DE-D- 68911742	10-02-94
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